REMARKS

A detailed listing of all claims that are under examination in the application is presented above, with an appropriate defined status identifier.

Claims 16-18, 20, 22, 25, and 27-30 are pending in the application, with claim 16 being the independent claim. Claim 16 is sought to be amended. Claims 20, 23 and 24 are sought to be canceled without prejudice to or disclaimer of the subject matter therein. Claims 1-15, 19, and 26 were cancelled by previous amendment.

Claim 16 has been amended to incorporate the elements of previously presented claim 23. Claim 23 is cancelled by the present amendment.

The amendment to claim 16 has been made to put the pending claims into better form for consideration on appeal, as required under 37 C.F.R. § 1.116(b)(2). Amended claim 16 was not presented earlier because Applicants believed that it was allowable in its previous form.

These changes are believed to introduce no new matter, and their entry is respectfully requested.

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. The Double Patenting Rejection

The Examiner provisionally rejects claims 16-18, 20-25, and 27-30 on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 7, 19, 20, 23, and 27 of co-pending Application No. 10/498,215. (Office Action, at page 2, lines 10-14.)

Claims 21, 23 and 24 are canceled by the present amendment, rendering the rejection moot with respect to these claims.

With respect to claims 16-18, 20, 22, 25 and 27-30, Applicants again respectfully request that the Examiner hold in abeyance the provisional obviousness-type double patenting rejection over claims 7, 19, 20, 23, and 27 of co-pending U.S. Appl. No. 10/498,215, which at present is being prosecuted and for which examination has not yet been concluded. When a provisional obviousness-type double patenting rejection is the only rejection remaining, the

Examiner should withdraw the rejection and allow the application to issue as a patent. *See* Manual of Patent Examining Procedure (MPEP), Eighth Ed., § 804, p. 800-17 (August 2007).

II. The Rejection of the Claims Under 35 U.S.C. § 103

The Examiner rejects claims 16-18, 20-25, and 27-30 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Okada *et al.*, U.S. Pat. No. 6,113,943 ("Okada") in view of Hutchinson, U.S. Pat. No. 5,889,110 ("Hutchinson"). Applicants respectfully traverse this rejection.

Specifically, the Examiner states that "Okada teaches a sustained release preparation comprising a polymer of lactic acid having an average molecular weight of about 25,000 to about 60,000 and a physiologically active peptide, wherein the peptide is leuprorelin . . . and which releases the physiologically active substance over a period of at least five months . . . ." but that "Okada does not teach a short term use of the sustained release preparation." (Office Action, at page 3, line 17, to page 4, line 5.) The Examiner continues, stating that Hutchinson "teaches extended release pharmaceutical compositions, [with] suitable pharmacologically active peptides such as LHRH, leuprorelin," "discloses experiments for release of goserelin over relatively short periods of time of 5-7 weeks" and "teaches a lactide/glycolide co-polymer having a weight average molecular weight of about 15,000 Da . . . ." (Office Action, at page 4, lines 6-11.) The Examiner concludes that "one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention" and, thus, "the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made . . . ." (Office Action, at page 4, lines 18-22.)

Applicants' invention as presently claimed is directed to a sustained release preparation comprising a combination of first microcapsules which gradually release a GnRH agonist or a salt thereof for 5 months or longer, and second microcapsules which gradually release a GnRH agonist or a salt thereof for shorter than 5 months so that blood concentration of the GnRH agonist within one week after administration is about 2 ng/mL or higher, wherein (a) the first microcapsules comprise (i) a GnRH agonist or a salt thereof, and (ii) a lactic acid polymer having a weight-average molecular weight of about 18,000 to about 30,000; and (b) the second microcapsules comprise (i) a GnRH agonist or a salt thereof, and (ii) a lactic acid-glycolic acid polymer (75/25 (mol %)) having a weight-average molecular

weight of 3,000 to about 12,000, or a lactic acid polymer having a weight-average molecular weight of about 13,000 to about 18,000.

Applicants submit that one of skill in the art, in light of Okada and Hutchinson, would not have arrived at the sustained release preparation as presently claimed, because a person skilled in the art would not have been motivated to combine Hutchinson with Okada.

Neither Okada nor Hutchinson teach or suggest a combination of two kinds of microcapsules of polymers having different weight average molecular weights to produce a sustained release preparation, as recited in Applicants' claims.

In addition, Okada teaches sustained release preparations containing lactic acid polymers having a weight average molecular weight higher than that of the lactic acid polymers in Applicants' claimed sustained release preparation. As acknowledged by the Examiner, the lactic acid polymers in Okada's sustained release preparations have a weight average molecular weight range of about 25,000 to about 60,000 (Office Action, at page 3, lines 17-18). In contrast, the lactic acid polymers in the first microcapsules of Applicants' sustained release preparation have a weight average molecular weight of about 18,000-30,000, a range that is lower than that disclosed in Okada. The lactic acid polymers in the second microcapsules of Applicants' sustained release preparation also have a lower weight average molecular weight range (13,000-18,000) than that disclosed in Okada.

Hutchinson also teaches that the duration of peptide drug release is determined in part by the weight average molecular weight of the polyester (e.g., lactic acid polymer) in the sustained release preparation. See Hutchinson, at col. 16, lines 51-53. At column 16, line 58, to column 17, line 5, Hutchinson exemplifies the weight average molecular weights of polyester polymers used in sustained release compositions having short peptide release periods of from 1 to 4 months, as opposed to those having longer release periods of greater than 6 months. For example, Hutchinson discloses that for sustained release compositions having a duration of peptide drug release of from one to four months, compositions comprising polyesters having a weight average molecular weight from 4,000 to 20,000 are preferred, whereas for compositions having longer release periods, for example, greater than six months, polyesters having weight average molecular weights of 20,000 to 50,000 are preferred. Hutchinson, at col. 16, line 58, to col. 17, line 5.

From this, Applicants believe that a person skilled in the art would have readily understood from Hutchinson that the sustained release effect is greatly influenced by the difference in weight average molecular weight of the component polymers of a sustained release preparation, and that selecting component polymers having a particular weight average molecular weight would produce the desired sustained release period for the preparation.

Hutchinson thus appears to suggest that the drug release period of a sustained release preparation can be controlled by changing the weight average molecular weight of the polyester (e.g., lactic acid polymer) in the sustained release preparation, and can be seen as teaching away from the idea of producing sustained release preparations by combining two kinds of microcapsules, each containing polymers having the weight average molecular weight ranges recited in the present claims.

Moreover, Applicants note that even if Okada and Hutchinson were combined, they still would not teach or suggest the advantages of the present invention as shown in the experiments in the specification (e.g., at page 83, line 15, to page 85, line 18, in Experimental Examples 1-3.)

Accordingly, Applicants believe that a person skilled in the art, at the time the invention was made, would not have been motivated to combine Hutchinson with Okada to arrive at the claimed sustained release preparations. Thus, in view of these two references, Applicants' sustained release preparations as currently claimed would not have been *prima facie* obvious to one of ordinary skill in the art.

Applicants submit that the rejection of claims 16-18, 20-25, and 27-30 under 35 U.S.C. § 103(a) has been overcome and respectfully request that the Examiner withdraw the rejection.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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